1-year outcomes with the Absorb bioresorbable scaffold in patients with coronary artery disease: a patient-level, pooled meta-analysis

Gregg W Stone, Runlin Gao, Takeshi Kimura, Dean J Kereiakes, Stephen G Ellis, Yoshinobu Onuma, Wai-Fung Cheong, Jennifer Jones-McMeans, Xiaolu Su, Zhen Zhang, Patrick W Serruys

Summary

Background **Compared with metallic drug-eluting stents, bioresorbable vascular scaffolds (BVS) offer the potential to improve long-term outcomes of percutaneous coronary intervention. Whether or not these devices are as safe and effective as drug-eluting stents within the first year after implantation is unknown.**

Methods **We did a patient-level, pooled meta-analysis of four randomised trials in which 3389 patients with stable coronary artery disease or a stabilised acute coronary syndrome were enrolled at 301 academic and medical centres in North America, Europe, and the Asia-Pacific region. These patients were randomly assigned to the everolimus-eluting Absorb BVS (n=2164) or the Xience cobalt-chromium everolimus-eluting stent (CoCr-EES; n=1225). The primary endpoints were the 1-year relative rates of the patient-oriented composite endpoint (all-cause mortality, all myocardial infarction, or all revascularisation) and the device-oriented composite endpoint of target lesion failure (cardiac mortality, target vessel-related myocardial infarction, or ischaemia-driven target lesion revascularisation). All analyses were by intention to treat. The four randomised trials included in our meta-analysis are all registered with ClinicalTrials.gov, numbers NCT01751906, NCT01844284, NCT01923740, and NCT01425281.**

Findings **The summary treatment effect for the 1-year relative rates of the patient-oriented composite endpoint did not differ significantly different between BVS and CoCr-EES (relative risk [RR] 1·09 [0·89–1·34], p=0·38). Similarly, the 1-year relative rates of the device-oriented composite endpoint did not differ between the groups (RR 1·22 [95% CI 0·91–1·64], p=0·17). Target vessel-related myocardial infarction was increased with BVS compared with CoCr-EES (RR 1·45 [95% CI 1·02–2·07], p=0·04), due in part to non-significant increases in peri-procedural myocardial infarction and device thrombosis with BVS (RR 2·09 [0·92–4·75], p=0·08). The relative rates of all-cause and cardiac mortality, all myocardial infarction, ischaemia-driven target lesion revascularisation, and all revascularisation did not differ between BVS and CoCr-EES. Results were similar after multivariable adjustment for baseline imbalances, and were consistent across most subgroups and in sensitivity analysis when two additional randomised trials with less than 1 year of follow-up were included.**

Interpretation **In this meta-analysis, BVS did not lead to different rates of composite patient-oriented and device-oriented adverse events at 1-year follow-up compared with CoCr-EES.**

Funding **Abbott Vascular.**

Published **Online** January 26, 2016 http://dx.doi.org/10.1016/S0140-6736(15)01039-9

New York Presbyterian Hospital, Columbia University Medical Center, New York, NY, USA (Prof G W Stone MD); **Cardiovascular Research Foundation, New York, NY, USA** (Prof G W Stone); **Fu Wai Hospital, National Center for Cardiovascular Diseases, Chinese Academy of Medical Sciences, Beijing, China** (Prof R Gao MD); **Kyoto University Hospital, Kyoto, Japan** (T Kimura MD); **The Christ Hospital, Heart and Vascular Center, Lindner Research Center, Cincinnati, OH, USA** (D J Kereiakes MD); **Cleveland Clinic, Cleveland, OH, USA** (Prof S G Ellis MD); **Thoraxcenter, Erasmus Medical Center, Rotterdam, Netherlands** (Y Onuma PhD); **Abbott Vascular, Santa Clara, CA, USA** (W-F Cheong PhD, J Jones-McMeans PhD, X Su MS, Z Zhang PhD); **and International Centre for Cardiovascular Health, Imperial College, London, UK** (Prof P W Serruys PhD)

Correspondence to:
Prof Gregg W Stone, Columbia University Medical Center, The Cardiovascular Research Foundation, 111 E 59th St, 11th Floor, New York, NY 10022, USA
gs2184@columbia.edu

Introduction

As technology has advanced from balloon angioplasty to bare metal stents to drug-eluting stents, patient outcomes after percutaneous coronary intervention have progressively improved, especially within the first year after treatment.[1–3] However, all metallic stents remain susceptible to very late (>1 year) stent thrombosis and restenosis, which limits long-term event-free survival and means that many patients have chronic reliance on dual anti-platelet therapy.[2–7] In many large-scale randomised trials, adverse events adjudicated as originating from the treated target lesion after metallic drug-eluting stents occur at a rate of 2–3% per year for at least 5 years, with no plateau evident.[4–6] Such events are thought to arise in large part from the permanent presence of a metallic endoprosthesis at the target lesion site. Fully bioresorbable vascular scaffolds (BVS) were therefore developed to provide the drug delivery and mechanical support functions of metallic drug-eluting stents within the first year, and then completely resorb within the next few years (being replaced by cellular and connective tissue), thereby restoring vascular function and improving long-term patient outcomes.

The Absorb BVS (Abbott Vascular, Santa Clara, CA, USA; hereafter referred to as BVS), is a 150 μm thick bioresorbable poly(L-lactide) scaffold with a conformal bioresorbable poly(D,L-lactide) coating (total thickness 7 μm) that elutes everolimus. Randomised trials comparing this device to the Xience cobalt-chromium everolimus-eluting stent (CoCr-EES; Abbott Vascular) were done to support regulatory approval in Europe, Asia, and the USA, and have only recently been reported.[8–11] These studies were designed to show the non-inferiority of BVS compared with CoCr-EES for

Research in context

Evidence before this study

We searched PubMed, several websites (www.tctmd.com, www.clinicaltrials.gov, www.clinicaltrialresults.org, and www.acc.org) and the proceedings of major cardiology meetings within the past 5 years (Jan 1, 2010–Oct 1, 2015) to identify randomised trials of bioresorbable vascular scaffolds (BVS) versus metallic drug-eluting stents. We did not use any language restrictions in our search. We identified six candidate trials: ABSORB II, ABSORB Japan, ABSORB China, ABSORB III, EVERBIO II, and TROFI II. Individual review of these trials showed non-significantly different 1-year outcomes between the everolimus-eluting Absorb BVS and the Xience cobalt-chromium everolimus-eluting stent (CoCr-EES) for most clinical endpoints, with some exceptions (lower all-cause mortality with BVS *vs* CoCr-EES in ABSORB China, and greater subacute device thrombosis between 1 and 30 days with BVS than with CoCr-EES in ABSORB III). However, only two of these trials were powered for clinical endpoints (ABSORB III and ABSORB Japan) and none were sufficiently large to detect differences in low-frequency endpoints between BVS and CoCr-EES.

Added value of this study

This patient-level, pooled meta-analysis of four trials in 3389 randomly assigned patients provides substantially greater power to describe the safety and effectiveness profile of BVS versus CoCr-EES than any of the individual studies alone. Our analysis shows similar results for BVS and CoCr-EES for the patient-oriented composite endpoint and the device-oriented composite endpoint at 1 year, which are arguably the most important overall measures of patient-related and device-related clinical outcomes. These findings were similar if the two additional randomised trials with less than 1 year follow-up (EVERBIO II and TROFI II) were added. An increase in target vessel-related myocardial infarction with BVS was observed, which might be attributable to non-significant increases in peri-procedural myocardial infarction and device thrombosis, although no differences between the groups were noted in cardiac or all-cause mortality, all myocardial infarction, or revascularisation measures of efficacy.

Implications of all the available evidence

Despite BVS being a first-generation technology for which most users are still learning the optimum implantation technique, and despite the fact that in these trials BVS was compared against CoCr-EES—the metallic drug-eluting stent with the lowest rate of stent thrombosis—the aggregate of available evidence supports the safety and effectiveness of BVS at 1 year for treatment of patients with stable coronary artery disease and stabilised acute coronary syndromes. Attention to appropriate device sizing, adequate lesion preparation, and routine high-pressure post-dilatation might further improve the 30-day and 1-year outcomes of BVS. Long-term results from the present and additional ongoing large-scale trials are needed to ascertain whether or not the novel properties of BVS result in improved late outcomes in patients with coronary artery disease undergoing percutaneous coronary intervention.

1-year clinical and angiographic outcomes, since improved results with BVS compared with drug-eluting stents are not expected to become evident until 3–5 years after implantation. However, none of these trials were powered to exclude small differences in composite adverse event rates between devices, or to detect differences in rarely occurring safety endpoints, and their outcomes according to specific patient and lesion characteristics are unknown. To further characterise the relative risks and benefits of BVS, we therefore did a patient-level, pooled meta-analysis of completed randomised trials of BVS.

Methods

Study design and participants

For inclusion in this meta-analysis, we identified all randomised trials of the Absorb BVS versus Xience CoCr-EES in patients with stable coronary artery disease or stabilised acute coronary syndromes in whom at least 1 year of clinical follow-up was available. We identified relevant studies by searching MEDLINE, several websites (www.tctmd.com, www.clinicaltrials.gov, www.clinicaltrialresults.org, and www.acc.org), and abstracts and presentations from major cardiovascular meetings using the keywords "randomised clinical trial", "drug-eluting stent", "everolimus-eluting stent", and "bioabsorbable (or "bioresorbable") scaffold" (or "stent"). Four trials met these criteria: ABSORB II,[8] ABSORB Japan,[9] ABSORB China,[10] and ABSORB III[11] (ClinicalTrials.gov identifiers: NCT01751906, NCT01844284, NCT01923740, and NCT01425281, respectively). We also identified two randomised trials that were not included in the primary analysis: EVERBIO II (follow-up only through 9 months)[12] and TROFI II (enrolment limited to patients with ST-segment elevation myocardial infarction, and follow-up only through 6 months).[13] The sponsor of the four ABSORB trials (Abbott Vascular) and the principal investigators of each study agreed to the data being pooled in a common database. Each study was approved by the institutional review board or ethics committee at each participating centre, and all patients signed informed, written consent before randomisation.

Outcomes and definitions

The main endpoints for this analysis were the patient-oriented composite endpoint (all-cause mortality, all myocardial infarction, or all revascularisation) and the device-oriented composite endpoint of target lesion failure (cardiac mortality, target vessel-related myocardial infarction, or ischaemia-driven target lesion

revascularisation). Mortality was subclassified as cardiac or non-cardiac in origin; if its cause could not be determined, it was classified as cardiac mortality. Peri-procedural myocardial infarction was defined as an increase in creatine kinase isoenzyme MB (CK-MB) to more than five-times the upper limit of normal within 48 h after percutaneous coronary intervention. Peri-procedural myocardial infarction was also determined through the use of the Society of Cardiac Angiography and Interventions definition of a clinically relevant myocardial infarction.[14] Spontaneous myocardial infarction, ischaemia-driven target lesion revascularisation, and ischaemia-driven target vessel revascularisation were otherwise defined consistently across studies.[15] Device thrombosis was defined according to the Academic Research Consortium definite or probable criteria.[16] Device success (at the lesion level) was defined as successful delivery and deployment of the study device at the intended target lesion with attainment of a final in-device diameter stenosis of up to 30% by quantitative coronary angiography (or by visual estimate if quantitative coronary angiography was unavailable). Procedural success (at patient level) was defined as achievement of a final in-device diameter stenosis of up to 30% by quantitative coronary angiography (or by visual estimate if quantitative coronary angiography was unavailable), with successful delivery and deployment of at least one study scaffold or stent at each intended target lesion without the occurrence of target lesion failure during the hospital stay (for a maximum of 7 days).

All ischaemic endpoints were adjudicated in each study by an independent clinical events committee masked to device assignment after source document review. Quantitative coronary angiography of the acute procedural results was done in each study by an independent core laboratory, with results reported within the confines of the device (in-device) and over the device length plus 5 mm proximal and distal margins (in-segment), as described previously.[17]

Statistical analysis

The main aims of this study were: to do a meta-analysis of the four included studies, deriving summary treatment effect estimates for the endpoints of interest; to generate time-to-event curves and explore the temporal differences in event rates between devices, with use of landmark analysis where appropriate; to analyse the univariable and multivariable determinants of 1-year adverse events; and to explore the consistency of the major endpoints across clinically relevant subgroups. To examine whether or not the main results would be changed by the addition of the TROFI II and EVERBIO II studies, we also ascertained the study-level treatment effects for all six trials in a post-hoc sensitivity analysis.

We studied the overall estimate of treatment effects using a Mantel-Haenszel fixed-effects model, which is preferred to a random-effects model when few events (<5) occur in any of the treatment groups in the component trials (as was the case for several endpoints, eg, device thrombosis).[18] This model provides similar results to an inverse variance-weighted model for non-zero events. We used relative risks (RRs) and 95% CIs as summary statistics. We assessed heterogeneity between trials with Cochran's Q test and the I^2 statistic, in which values lower than 25% indicate low heterogeneity, 25–50% represent moderate heterogeneity, and 50% or higher indicate high heterogeneity.

	ABSORB II[8]	ABSORB Japan[9]	ABSORB China[10]	ABSORB III[11]
ClinicalTrials.gov identifier	NCT01425281	NCT01844284	NCT01923740	NCT01751906
Centres, n	46	38	24	193
Randomised patients, n	501	400	480	2008
Assigned to BVS, n	335	266	241	1322
Assigned to CoCr-EES, n	166	134	239	686
Study lesions allowed, n	2	2	2	2
Study vessels allowed, n*	2	2	2	2
Target lesion reference vessel diameter	Maximum lumen diameter 2·25 to 3·8 mm by online QCA	≥2·5 to ≤3·75 mm by online QCA or visual assessment	≥2·5 to ≤3·75 mm by online QCA or visual assessment	≥2·5 to ≤3·75 mm by visual assessment (QCA or imaging allowed)
Target lesion length	≤48 mm	≤24 mm	≤24 mm	≤24 mm
Device overlap allowed?	Yes	For bailout only	For bailout only	For bailout only
1-year clinical follow-up complete	493 (98%)	397 (99%)	475 (99%)	1990 (99%)
Routine angiographic follow-up	At 3 years	At 13 months	At 1 year	No
Primary endpoint	Angiographic vasomotion at 3 years	Target lesion failure at 1 year	Angiographic in-segment late loss at 1 year	Target lesion failure at 1 year
Total duration of follow-up	5 years	5 years	5 years	5 years

BVS=Absorb bioresorbable vascular scaffold. CoCr-EES=XIENCE cobalt-chromium everolimus-eluting stent. QCA=quantitative coronary angiography. *Maximum one lesion per vessel.

Table 1: **Major characteristics of the four randomised trials**

	BVS (n=2164)	CoCr-EES (n=1225)	p value
Age, years	63 (56–71)	63 (56–70)	0·25
Male sex	1568/2161 (73%)	884/1223 (72%)	0·86
Body-mass index, kg/m²	28·8 (5·9)	28·5 (5·7)	0·17
Diabetes mellitus	652/2159 (30%)	367/1223 (30%)	0·91
Insulin-treated	207/2159 (10%)	120/1223 (10%)	0·83
Hypertension (medically treated)	1622/2161 (75%)	902/1223 (74%)	0·40
Hyperlipidaemia (medically treated)	1540/2161 (71%)	847/1223 (69%)	0·22
Current smoking	491/2161 (23%)	291/1223 (24%)	0·48
Previous percutaneous coronary intervention	716/2161 (33%)	372/1221 (31%)	0·11
Previous coronary artery bypass graft surgery	69/2161 (3%)	31/1221 (3%)	0·28
Previous myocardial infarction	457/2143 (21%)	268/1218 (22%)	0·65
Renal insufficiency*	145/1557 (9%)	76/922 (8%)	0·37
Pre-percutaneous coronary intervention evidence of ischaemia			
Silent ischaemia	253/2160 (12%)	126/1223 (10%)	0·21
Stable angina	1194/2160 (55%)	652/1223 (53%)	0·27
Unstable angina	603/2160 (28%)	379/1223 (31%)	0·06
Recent myocardial infarction	66/2160 (3%)	49/1223 (4%)	0·14
Post-myocardial infarction angina	16/2160 (1%)	8/1223 (1%)	0·77
None	28/2160 (1%)	9/1223 (1%)	0·13
Aspirin†	2108/2161 (98%)	1183/1223 (97%)	0·16
Platelet P2Y12 receptor inhibitor use†	2129/2161 (99%)	1198/1223 (98%)	0·22
Clopidogrel or ticlopidine	1615/2129 (76%)	945/1198 (79%)	0·047
Prasugrel or ticagrelor	514/2129 (24%)	253/1198 (21%)	0·047
Glycoprotein IIb/IIIa inhibitor use	148/1895 (8%)	98/1089 (9%)	0·26

Data are median (IQR), n/N (%), or mean (SD). BVS=Absorb bioresorbable vascular scaffold. CoCr-EES=XIENCE cobalt-chromium everolimus-eluting stent. *Estimated glomerular filtration rate <30 mL/min per 1·73 m² or dialysis at the time of screening. †Index procedure loading dose.

***Table 2*: Baseline clinical features and antiplatelet drugs (pooled across the four trials)**

All analyses are by intention to treat. For all studies, 1-year follow-up included a window of 28 days on either side of 1 year. Patients were included in the 1-year follow-up analysis if 1-year follow-up was complete or if an event occurred before 1 year. We ascertained the univariate correlates of selected 1-year adverse events using the Wald χ^2 test, adjusted by study. Independent predictors of 1-year adverse events were determined by multivariable logistic regression using backward selection, adjusted by study, with the number of variables for each model carefully chosen (according to their historical association with each event in previous studies) to avoid overfitting (around ten variables per event).[19] Pearson's goodness-of-fit test verified that each of the models was stable.

Demographic and baseline characteristics are summarised by treatment group, as means and SDs for continuous variables and as numbers and percentages for categorical variables. We compared continuous data using the *t* test, and binary data using Pearson's χ^2 test or Fisher's exact test. Time-to-first-event curves were displayed using Kaplan-Meier estimates, adjusted by study, with between-group differences compared by the Wald χ^2 test. The consistency of the treatment effect on selected endpoints in relevant subgroups (adjusted for study level) was assessed with formal interaction testing. We used metafor (version 1.9-7) in R version 3.2 to do the meta-analysis.[20,21] For all other statistical analyses, we used SAS version 9.2.

See Online for appendix

Role of the funding source

The ABSORB trials and the present meta-analysis were funded by Abbott Vascular (Santa Clara, CA, USA). The funder was involved in data analysis for the present study. GWS directed the present analysis and had full access to all the data, prepared the report, and had final responsibility for the decision to submit for publication. The funder had the right to review but not approve the final report.

Results

In the four trials, a total of 3389 patients were enrolled at 301 centres from North America, Europe, and the Asia-Pacific region (table 1), of whom 2164 were randomly assigned to BVS and 1225 to CoCr-EES. Tables 2 and 3 show the baseline clinical and angiographic features according to randomly assigned device (pooled across the four trials), and appendix pp 3–4 show the baseline features by trial (pooled across randomisation). Baseline characteristics were well matched between the two groups. Around 30% of patients had diabetes mellitus and about 31% presented with unstable angina or recent myocardial infarction (table 2). Two-thirds of target lesions were

	BVS (n=2164 patients, n=2275 lesions)	CoCr-EES (n=1225 patients; n=1284 lesions)	p value
Lesions treated, n (any)*	1·1 (0·4)	1·2 (0·4)	0·69
Target lesions treated, n	1·1 (0·2)	1·0 (0·2)	0·72
One target lesion	2045/2164 (95%)	1162/1225 (95%)	0·66
Two target lesions	115/2164 (5%)	61/1225 (5%)	0·67
Target coronary artery (lesion level)			
Left main	1/2275 (<1%)	0	1·0
Left anterior descending	1046/2275 (46%)	575/1284 (45%)	0·49
Left circumflex	581/2275 (26%)	357/1284 (28%)	0·14
Right	647/2275 (28%)	352/1284 (27%)	0·51
Lesion characteristics (lesion level)			
Calcification (moderate or severe)	623/2267 (28%)	339/1277 (27%)	0·55
Tortuosity (moderate or severe)	103/2268 (5%)	59/1277 (5%)	0·91
Eccentric	1823/2267 (80%)	1014/1273 (80%)	0·59
Bifurcation†	751/2268 (33%)	449/1274 (35%)	0·20
Thrombus	8/2268 (<1%)	4/1275 (<1%)	1·0
ACC/AHA class B2/C	1511/2270 (67%)	887/1276 (70%)	0·07
Quantitative measures (lesion level)			
Reference vessel diameter, mm	2·68 (0·44)	2·69 (0·46)	0·27
Minimum luminal diameter, mm	0·96 (0·37)	0·95 (0·36)	0·58
Diameter stenosis, %	64·1% (12·4)	64·6% (12·0)	0·26
Lesion length, mm	13·1 (5·6)	13·4 (5·7)	0·09

Data are mean (SD) or n/N (%). BVS=Absorb bioresorbable vascular scaffold. CoCr-EES=XIENCE cobalt-chromium everolimus-eluting stent. ACC=American College of Cardiology. AHA=American Heart Association. *Randomised target lesions plus non-randomised non-target lesions in a separate epicardial coronary artery. †Defined by the angiographic core laboratory as having a side branch with diameter ≥1·5 mm. The protocol of each study excluded bifurcation lesions with a side branch diameter ≥2·0 mm by visual estimate.

Table 3: **Baseline angiographic features (core laboratory assessments), pooled across the four trials**

classified by the core laboratory as American College of Cardiology or American Heart Association type B2 or C, more than a quarter were moderately or severely calcified, and roughly a third were bifurcation lesions (table 3). Quantitative measures of target lesion length, severity, and reference vessel diameter were similar between patients randomly assigned to BVS and CoCr-EES (table 3).

Procedural and angiographic results for the randomised groups are shown in table 4, and for each trial in appendix p 5. Despite similar lesion length, total device length was shorter for BVS than for CoCr-EES, although maximum device diameter and inflation pressures per lesion were similar. Post-dilatation was done more frequently and intravascular imaging guidance was slightly more common with BVS than with CoCr-EES. According to quantitative coronary angiography, in-device acute gain in minimal luminal diameter was smaller with BVS than with CoCr-EES and the final diameter stenosis was greater with BVS than CoCr-EES, although post-percutaneous coronary intervention in-segment diameter stenosis measurements were nearly identical with both devices (table 4). Device success per lesion and procedural success per patient were lower with BVS than with CoCr-EES (table 4).

1-year follow-up was complete in 3355 (99%) of 3389 patients. Aspirin, adenosine diphosphate antagonist, and combined dual anti-platelet therapy use were similar between the groups, although the more potent agents ticagrelor and prasugrel were used more frequently with BVS than with CoCr-EES (appendix p 6). The number of events in the pooled device groups and the summary meta-analysis statistics for 21 ischaemic endpoints are shown in table 5. The individual meta-analyses are shown in appendix pp 22–42. Figure 1 shows selected time-to-event Kaplan-Meier curves. The summary treatment effect for the 1-year relative rates of the patient-oriented composite endpoint of death, myocardial infarction, or revascularisation did not differ significantly between BVS and CoCr-EES (RR 1·09 [95% CI 0·89–1·34], p=0·38; table 5). Similarly, the 1-year relative rates of the device-oriented composite endpoint (target lesion failure) did not differ between the two devices (RR 1·22 [95% CI 0·91–1·64], p=0·17). However, target lesion failure tended to be higher with BVS than with CoCr-EES within 30 days, whereas target lesion failure rates were similar between the two devices between 30 days and 1 year (table 5). The relative rates of cardiac and all-cause mortality and all myocardial infarction (including peri-procedural or non-periprocedural myocardial infarction, and non-target vessel-related myocardial infarction) did not differ significantly between the two devices, although target vessel-related myocardial infarction was greater with BVS than with CoCr-EES (table 5). A detailed classification

	BVS (n=2164 patients, n=2275 lesions)	CoCr-EES (n=1225 patients, n=1284 lesions)	p value
Study devices per patient, n	1·1 (0·4)	1·1 (0·4)	0·98
Total device length per lesion, mm	18·8 (6·9)	19·6 (7·1)	0·0008
Overlapping study devices per lesion	159/2275 (7·0%)	95/1284 (7·4%)	0·65
Maximum device diameter per lesion, mm*	3·17 (0·41)	3·16 (0·43)	0·36
Maximum device pressure per lesion, atmospheres*	15·5 (3·2)	15·7 (3·3)	0·28
Post-dilatation done (per lesion)	1505/2275 (66·2%)	710/1284 (55·3%)	<0·0001
Bailout device used (per lesion)	101/2275 (4·4%)	72/1284 (5·6%)	0·12
Intravascular ultrasound or optical coherence tomography guidance (per procedure)	512/2141 (23·9%)	246/1210 (20·3%)	0·02
Post-percutaneous coronary intervention quantitative measures (lesion level)			
Reference vessel diameter, mm	2·71 (0·44)	2·75 (0·45)	0·02
In-device			
Acute gain, mm	1·41 (0·45)	1·58 (0·43)	<0·0001
Minimal luminal diameter, mm	2·37 (0·39)	2·53 (0·40)	<0·0001
Diameter stenosis, %	12·4% (8·3)	7·5% (8·2)	<0·0001
In-segment			
Acute gain, mm	1·20 (0·45)	1·24 (0·45)	0·04
Minimal luminal diameter, mm	2·16 (0·40)	2·19 (0·43)	0·07
Diameter stenosis, %	19·9% (7·7)	19·9% (8·4)	0·96
Procedure duration, min	43·7 (23·7)	39·7 (21·5)	<0·0001
Device success (per lesion)	2144/2243 (95·6%)	1265/1272 (99·4%)	<0·0001
Procedure success (per patient)	2038/2148 (94·9%)	1176/1212 (97·0%)	0·003

Data are mean (SD) or n/N (%). BVS=Absorb bioresorbable vascular scaffold. CoCr-EES=XIENCE cobalt-chromium everolimus-eluting stent. *Device delivery system or post-dilatation balloon.

Table 4: **Procedural and angiographic results (core laboratory assessments), pooled across the four trials**

of the underlying causes of target vessel-related myocardial infarction in the two groups is in appendix p 7. Definite or probable device thrombosis at 1 year was slightly more common with BVS than with CoCr-EE, although this difference was not statistically significant (table 5). Effectiveness measures, including ischaemia-driven target lesion revascularisation, ischaemia-driven target vessel revascularisation, and all revascularisation, occurred at similar frequency in the BVS and CoCr-EES groups (table 5). No significant heterogeneity between the four studies was present for any of the assessed endpoints (table 5). The main study-level treatment effects were similar in a sensitivity analysis in which the TROFI II and EVERBIO II trials were added to the four ABSORB trials (appendix pp 8–15).

Appendix pp 16–21 show the significant unadjusted correlates of selected adverse events. Multivariable analysis showed no significant differences in the 1-year rates of the patient-oriented composite endpoint, device-oriented composite endpoint, myocardial infarction, ischaemia-driven target lesion revascularisation, or device thrombosis between BVS and CoCr-EES, although target vessel-related myocardial infarction was higher with BVS than with CoCr-EES (table 6). We noted no significant interactions between treatment effects and most subgroups for the 1-year relative rates of the patient-oriented composite endpoint, except for diabetes (CoCr-EES tended to perform better in non-diabetic patients, but not in diabetic patients) and reference vessel diameter (CoCr-EES tended to perform better in larger vessels but not in smaller vessels; figure 2). We recorded no significant interactions between treatment effects and most subgroups for the 1-year relative rates of the device-oriented composite endpoint of target lesion failure, except for American College of Cardiology–American Heart Association lesion class (CoCr-EES tended to perform better in non-complex A/B1 lesions but not in more complex B2/C lesions; figure 3).

Discussion

In this patient-level, pooled meta-analysis from four randomised trials of the Absorb BVS versus the Xience CoCr-EES in 3389 patients with stable coronary artery disease and stabilised acute coronary syndromes, the overall relative rates of composite patient-oriented and device-oriented adverse events did not differ significantly between the two stents at 1-year follow-up. Target vessel-related myocardial infarction was more common with BVS than with CoCr-EES, although rates of all myocardial infarction, cardiac mortality, and all-cause mortality did not differ between the groups. Revascularisation measures of efficacy at 1 year were also similar between the two devices.

Very late restenosis and thrombosis are ongoing concerns after drug-eluting stent implantation. The permanent rigid frame common to all metallic stents

	BVS (n=2164)	CoCr-EES (n=1225)	Fixed-effects RR (95% CI)	p value	I^2	p value for heterogeneity
Patient-oriented composite endpoint (mortality, myocardial infarction, or revascularisation)	255/2147 (11·9%)	129/1212 (10·6%)	1·09 (0·89–1·34)	0·38	5·1%	0·37
Device-oriented composite endpoint (target lesion failure)	141/2147 (6·6%)	63/1212 (5·2%)	1·22 (0·91–1·64)	0·17	0%	0·78
Early (0–30 days)	89/2154 (4·1%)	32/1222 (2·6%)	1·49 (1·00–2·22)	0·051	0%	0·91
Late (30 days–1 year; landmark)	53/2140 (2·5%)	31/1211 (2·6%)	0·97 (0·62–1·51)	0·90	0%	0·84
All-cause mortality	17/2147 (0·8%)	9/1212 (0·7%)	1·12 (0·47–2·69)	0·80	NA	NA
Cardiac	8/2147 (0·4%)	4/1212 (0·3%)	1·26 (0·33–4·82)	0·74	NA	NA
Non-cardiac	9/2147 (0·4%)	5/1212 (0·4%)	1·02 (0·32–3·25)	0·97	NA	NA
All myocardial infarction	123/2147 (5·7%)	49/1212 (4·0%)	1·34 (0·97–1·85)	0·08	0%	0·71
Peri-procedural (Absorb III definition)	62/2126 (2·9%)	26/1196 (2·2%)	1·29 (0·82–2·03)	0·27	0%	0·75
Peri-procedural (SCAI definition)	16/2126 (0·8%)	9/1196 (0·8%)	0·97 (0·44–2·14)	0·94	0%	0·63
Non-peri-procedural (Absorb III definition)	61/2144 (2·8%)	22/1211 (1·8%)	1·48 (0·91–2·40)	0·11	0%	0·93
Target vessel-related myocardial infarction	110/2147 (5·1%)	40/1212 (3·3%)	1·45 (1·02–2·07)	0·04	0%	0·80
Non-target vessel-related myocardial infarction	15/2147 (0·7%)	11/1212 (0·9%)	0·75 (0·34–1·66)	0·48	0%	0·94
All revascularisation	169/2147 (7·9%)	93/1212 (7·7%)	1·02 (0·80–1·30)	0·89	21·9%	0·28
Ischaemia-driven target lesion revascularisation	57/2147 (2·7%)	28/1212 (2·3%)	1·14 (0·73–1·79)	0·56	0%	0·91
Ischaemia-driven target vessel revascularisation	92/2147 (4·3%)	45/1212 (3·7%)	1·14 (0·80–1·62)	0·47	11·2%	0·34
Device thrombosis (definite or probable)	28/2130 (1·3%)	7/1204 (0·6%)	2·09 (0·92–4·75)	0·08	0%	0·40
Definite	24/2130 (1·1%)	6/1204 (0·5%)	2·06 (0·85–5·03)	0·11	0%	0·84
Probable	4/2130 (0·2%)	1/1204 (0·1%)	2·28 (0·28–18·51)	0·44	NA	NA
Early (0–30 days)	20/2152 (0·9%)	6/1221 (0·5%)	1·76 (0·72–4·34)	0·22	0%	0·70
Late (30 days–1 year; landmark)	8/2128 (0·4%)	1/1204 (0·1%)	4·10 (0·52–32·56)	0·18	NA	NA

Data are n/N (%); the denominator in each cell is the number of eligible patients (1-year follow-up or earlier event). BVS=Absorb bioresorbable vascular scaffold. CoCr-EES=XIENCE cobalt-chromium everolimus-eluting stent. RR=risk ratio. NA=not applicable (cannot test for heterogeneity because no events were present in one cell in three of the four trials). SCAI=Society of Cardiovascular Angiography and Interventions.

Table 5: **Meta-analysis summary for all ischaemic endpoints**

straightens and fixes the external dimension of the vessel, eliminates beneficial flow-related and pressure-related vascular effects, and serves as a nidus for persistent inflammation, neoatherosclerosis, and strut fracture.[22–25] By contrast, BVS are more conformable than metallic drug-eluting stents, and restore cyclic pulsatility by 6 months and vasomotor responses by 12 months.[26,27] Through the removal of the mechanical constraints of a metallic frame, BVS results in increased luminal dimensions over a 5-year period because of adaptive remodelling of the external elastic membrane, strut resorption, and plaque regression—changes that are not possible after implantation of a metallic drug-eluting stent.[28,29] Formation of a protective 150–200 μm thick neointima after scaffold absorption might normalise endothelial shear stress and stabilise the lesion site.[30,31] Complete device bioresorption and replacement with a contractile neomedia could thereby improve long-term outcomes compared with metallic drug-eluting stents. Removal of the nidus for late adverse events could be especially important for young patients with coronary artery disease undergoing percutaneous coronary intervention and in those presenting with acute coronary syndromes due to thrombosis of a lipid-rich plaque, in which metallic drug-eluting stents heal poorly.[32] Other potential benefits of BVS include avoidance of a so-called full metal jacket in diffuse disease (facilitating later bypass graft surgery if necessary), late unjailing of covered side branches (potentially reducing ischaemia and restoring access for future intervention), and compatibility with non-invasive CT angiographic imaging (through avoidance of the blooming artifact of metallic stents). Finally, the cultural, religious, or personal preference of avoiding a permanent implant is an important consideration for some patients.

Large-scale randomised trials (eg, the ABSORB IV trial in 5000 patients [ClinicalTrials.gov identifier NCT02173379]) are necessary to establish whether or not BVS implantation can improve the long-term prognosis of percutaneous coronary intervention compared with metallic drug-eluting stents. However, these results will not be available for many years, and in the meantime, use of this new technology needs evidence that overall patient outcomes are not compromised within the first year of implantation. This consideration is especially important because BVS is a first-generation technology with thicker struts than contemporary metallic drug-eluting stents, and needs greater attention to procedural technique to achieve optimum results. Strut fracture can occur with excessive over-dilatation, and under-expansion might be associated with increased risks of scaffold thrombosis and restenosis, especially in very small vessels. Even the largest study reported so far—the ABSORB III trial with

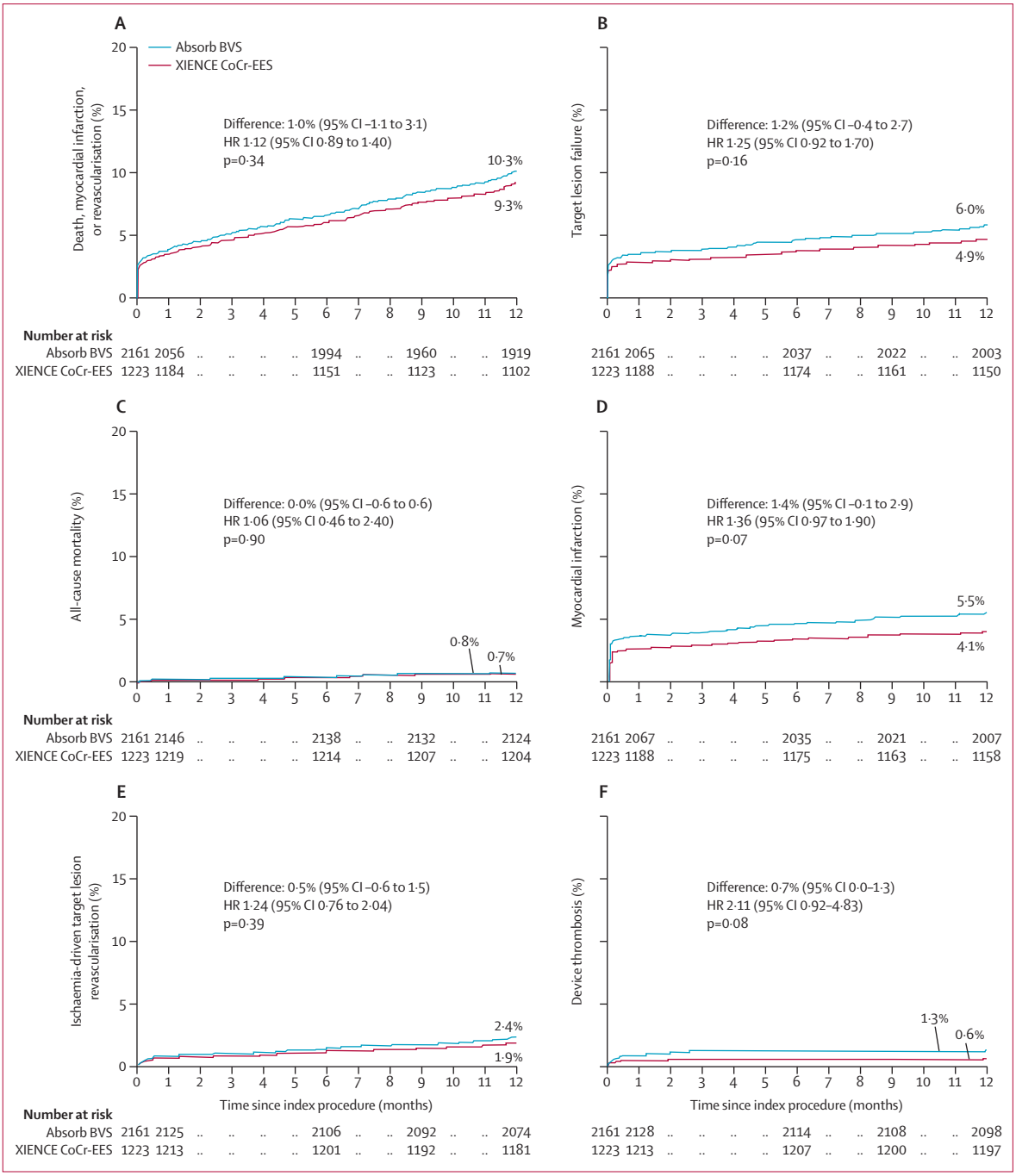

Figure 1: **Time-to-first event curves for patients randomly assigned to Absorb BVS versus XIENCE CoCr-EES**
The patient-oriented composite endpoint of death, myocardial infarction, or any revascularisation. (B) The device-oriented composite endpoint of target lesion failure (cardiac death, target vessel myocardial infarction, or ischaemia-driven target lesion revascularisation). (C) All-cause mortality. (D) All myocardial infarction. (E) Ischaemia-driven target lesion revascularisation. (F) Device thrombosis (definite or probable). Note that follow-up is censored at the time of first event, or at last follow-up or at exactly 12 months (whichever occurred later), and therefore these rates differ slightly from the binary event rates in table 5. BVS= bioresorbable vascular scaffold. CoCr-EES=cobalt-chromium everolimus-eluting stent. HR=hazard ratio.

2008 randomised patients[11]—was not sufficiently powered to exclude small clinically relevant differences between BVS and CoCr-EES within the first year, or to examine outcomes in subgroups.

We therefore did the present patient-level, pooled meta-analysis from four randomised trials with a total of 3389 patients to have greater power to detect differences in safety or effectiveness between BVS and

	Relative risk (95% CI)	p value
Patient-oriented composite endpoint (death, myocardial infarction, or revascularisation)		
Diabetes present	1·39 (1·15–1·68)	0·0008
Previous cardiac intervention	1·40 (1·16–1·69)	0·0006
Number of target lesions (≥2 *vs* 1)	1·45 (1·16–1·82)	0·001
Any lesion with minimal luminal diameter <median (0·93 mm)*	1·37 (1·13–1·68)	0·002
Any lesion with reference vessel diameter <median (2·65 mm)*	1·23 (1·01–1·51)	0·04
Any ACC/AHA class B2 or C lesion (*vs* class A or B1)*	1·38 (1·11–1·73)	0·003
BVS (*vs* CoCr-EES)	1·10 (0·90–1·34)	0·29
Device-oriented composite endpoint (target lesion failure: cardiac death, target vessel-related myocardial infarction, or ischaemia-driven target lesion revascularisation)		
Diabetes present	1·56 (1·19–2·04)	0·002
Previous cardiac intervention	1·36 (1·03–1·78)	0·03
Any lesion with minimum luminal diameter <median (0·93 mm)*	1·37 (1·03–1·82)	0·03
Any lesion with reference vessel diameter <median (2·65 mm)*	1·52 (1·14–2·03)	0·005
Any ACC/AHA class B2 or C lesion (*vs* class A or B1)*	1·65 (1·19–2·28)	0·002
BVS (*vs* CoCr-EES)	1·23 (0·92–1·64)	0·14
Myocardial infarction, all		
Diabetes present	1·61 (1·20–2·15)	0·002
Previous cardiac intervention	1·60 (1·19–2·15)	0·002
Number of target lesions (≥2 *vs* 1)	1·47 (1·03–2·08)	0·04
Any lesion with minimum luminal diameter <median (0·93 mm)*	1·42 (1·04–1·95)	0·03
Any lesion with reference vessel diameter <median (2·65 mm)*	1·57 (1·13–2·16)	0·007
Any ACC/AHA class B2 or C lesion (*vs* class A or B1)*	1·68 (1·18–2·41)	0·003
BVS (*vs* CoCr-EES)	1·35 (0·98–1·87)	0·052
Target vessel-related myocardial infarction		
Diabetes present	1·61 (1·17–2·20)	0·004
Any lesion with minimum luminal diameter <median (0·93 mm)*	1·44 (1·03–2·02)	0·03
Any lesion with reference vessel diameter <median (2·65 mm)*	1·73 (1·22–2·45)	0·002
Any ACC/AHA class B2 or C lesion (*vs* class A or B1)*	1·78 (1·21–2·63)	0·003
BVS (*vs* CoCr-EES)	1·44 (1·01–2·05)	0·04

(Table 6 continues in next column)

(Continued from previous column)

	Relative risk (95% CI)	p value
Ischaemia-driven target lesion revascularisation		
Diabetes present	2·53 (1·66–3·87)	<0·0001
Any lesion with reference vessel diameter <median (2·65 mm)*	1·95 (1·24–3·06)	0·004
Any lesion with moderate or severe calcification*	1·76 (1·14–2·70)	0·01
BVS (*vs* CoCr-EES)	1·08 (0·69–1·68)	0·73
Device thrombosis (definite or probable)		
Diabetes present	2·88 (1·49–5·60)	0·002
Any lesion with reference vessel diameter <median (2·65 mm)*	3·28 (1·50–7·20)	0·003
Any ACC/AHA class B2 or C lesion (*vs* class A or B1)*	2·91 (1·13–7·46)	0·03
BVS (*vs* CoCr-EES)	2·19 (0·96–4·98)	0·06

ACC=American College of Cardiology. AHA=American Heart Association. BVS=Absorb bioresorbable vascular scaffold. CoCr-EES=XIENCE cobalt-chromium everolimus-eluting stent. *Angiographic core laboratory determination. Device randomisation was forced into each model. The following additional variables were entered into the models for the patient-oriented composite endpoint, the device-oriented composite endpoint, all myocardial infarction, and target vessel-related myocardial infarction: age (median 63 years), sex, current smoking, hypertension, hyperlipidaemia, diabetes, previous myocardial infarction, previous cardiac intervention, presentation with unstable angina/recent myocardial infarction (*vs* stable ischaemic syndrome), number of target lesions (≥2 *vs* 1), platelet P2Y12 receptor inhibitor loading with prasugrel or ticagrelor (*vs* clopidogrel or ticlopidine), reference vessel diameter (any lesion <median 2·65 mm), minimum luminal diameter (any lesion <median 0·93 mm), lesion length (any lesion <median 12·16 mm), any ACC/AHA class B2/C lesion (*vs* class A/B1), any left anterior descending lesion, any lesion with moderate or severe calcification, and any bifurcation lesion. The following additional variables were entered into the models for ischaemia-driven target vessel revascularisation: diabetes, presentation with unstable angina or recent myocardial infarction, number of target lesions, platelet P2Y12 receptor inhibitor loading with prasugrel or ticagrelor, reference vessel diameter, minimum luminal diameter, lesion length, any ACC/AHA class B2/C lesion, any left anterior descending lesion, any lesion with moderate or severe calcification. The following additional variables were entered into the model for device thrombosis: diabetes, reference vessel diameter, lesion length, presentation with unstable angina or recent myocardial infarction, and any ACC/AHA class B2/C lesion.

Table 6: **Independent baseline predictors of 1-year ischaemic events by logistic regression**

CoCr-EES. By contrast with a standard study-level meta-analysis, a patient-level, pooled meta-analysis offers three important advantages: time-to-event curves (and landmark analysis) can be generated to elucidate the temporal sequence of events; multivariable analyses can be done to ascertain the individual predictors of outcomes; and the consistency of treatment effects can be analysed in clinically relevant subgroups.

The most important finding of the present study is that the 1-year rates of the patient-oriented composite endpoint of death, myocardial infarction, or revascularisation were similar with BVS and CoCr-EES. The 1-year rates of the device-oriented composite endpoint of cardiac death, target vessel-related myocardial infarction, or ischaemia-driven target lesion revascularisation also did not differ significantly with BVS and CoCr-EES. These outcomes were similar after multivariable adjustment for small differences in baseline variables, and when the TROFI II and EVERBIO II trials were included. Patient-related and device-related treatment effects were consistent across most clinically relevant subgroups analysed. These findings therefore provide reassurance that overall patient-related and device-related outcomes within the first year are not substantially compromised with use of BVS. These results are especially noteworthy because the comparator device in the four trials was the

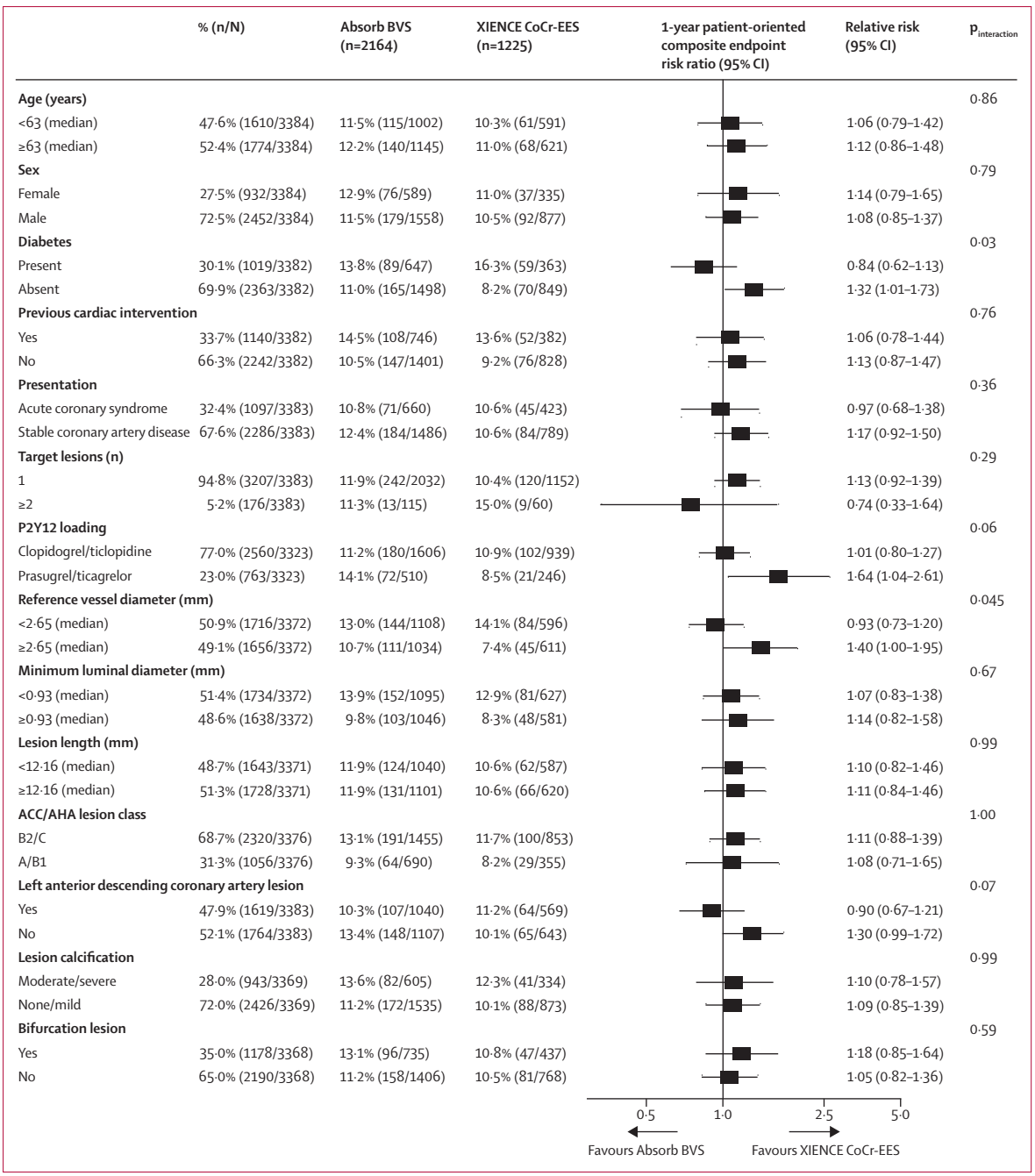

Figure 2: **Subgroup analyses for the pooled 1-year rates of the patient-oriented composite endpoint of all-cause mortality, all myocardial infarction, or all revascularisation in patients randomly assigned to BVS versus CoCr-EES**

The p value for interaction represents the likelihood of interaction between the variable and the relative treatment effect. BVS= bioresorbable vascular scaffold. CoCr-EES=cobalt-chromium everolimus-eluting stent. ACC=American College of Cardiology. AHA=American Heart Association.

CoCr-EES, which is the metallic drug-eluting stent associated with the lowest rate of stent thrombosis and greatest freedom from adverse events.[1–3] Additionally, BVS was used for the first time by most of the investigators in these studies, and historically interventional device-related outcomes have improved over time with increasing experience.

Nonetheless, some differences between devices were evident that warrant discussion. In particular, although overall rates of myocardial infarction were not significantly increased with BVS, target vessel-related myocardial infarction occurred more frequently with BVS than with CoCr-EES, due in part to non-significant increases in peri-procedural myocardial infarction and

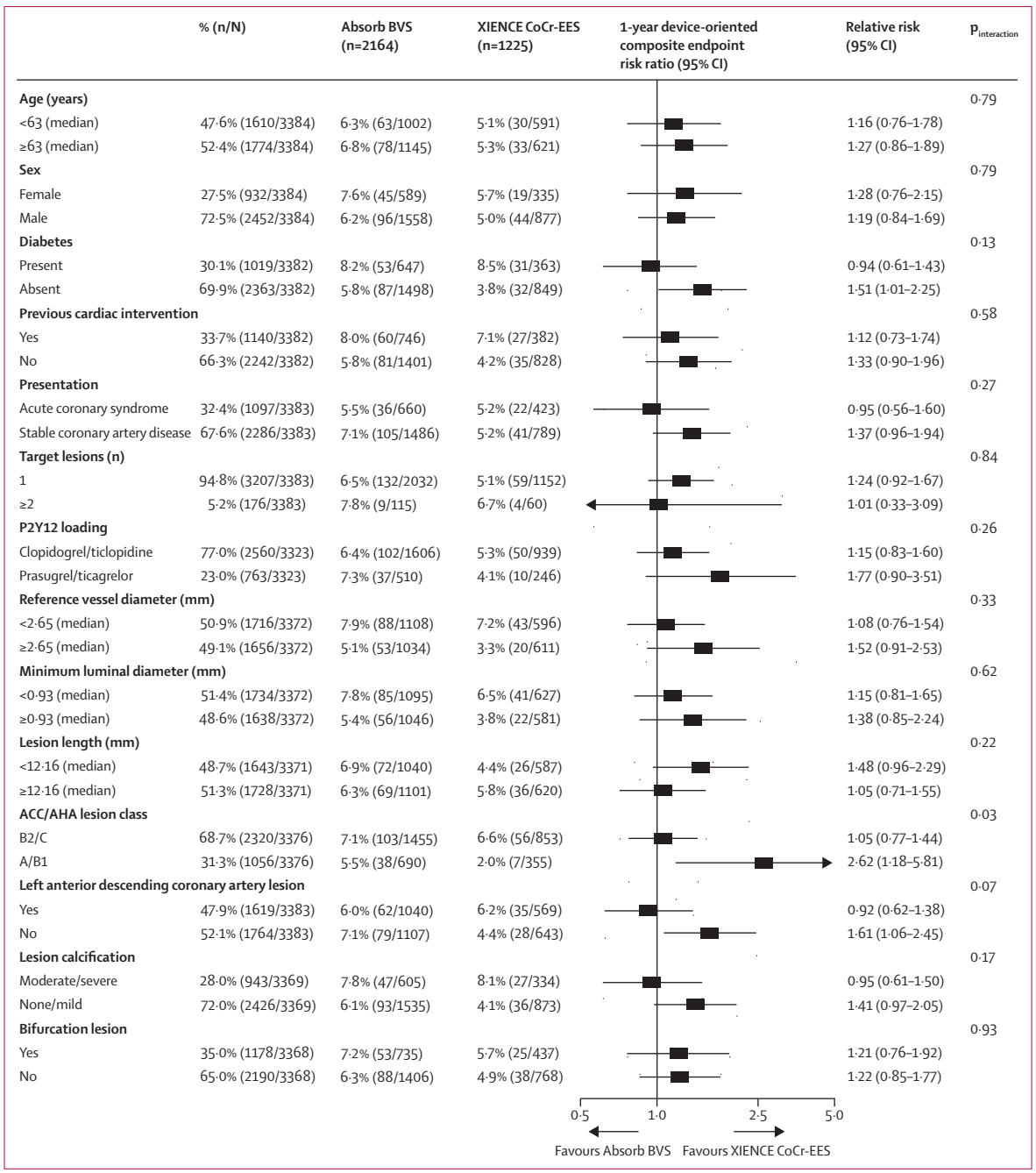

Figure 3: **Subgroup analyses for the pooled 1-year rates of the device-oriented composite endpoint of target lesion failure (cardiac mortality, target vessel-related myocardial infarction, or ischaemia-driven target lesion revascularisation) in patients randomly assigned to BVS versus CoCr-EES**
The p value for interaction represents the likelihood of interaction between the variable and the relative treatment effect. BVS= bioresorbable vascular scaffold. CoCr-EES=cobalt-chromium everolimus-eluting stent. ACC=American College of Cardiology. AHA=American Heart Association.

device thrombosis with BVS. However, most peri-procedural myocardial infarctions are not prognostically important,[14] and clinically relevant large peri-procedural myocardial infarction according to the Society of Cardiac Angiography and Interventions criteria occurred in only 0·8% of patients with each device. Although not significant, a 0·6% absolute increase in definite device thrombosis contributed to the 1·0% absolute difference in non-peri-procedural target vessel-related myocardial infarctions with BVS compared with CoCr-EES, with the remainder attributed to target vessel-related myocardial infarctions not related to device thrombosis. Device and procedure success rates were also somewhat lower with BVS than with CoCr-EES, and the greater strut thickness

and post-percutaneous coronary intervention in-device diameter stenosis with BVS than with CoCr-EES might have contributed to these target vessel myocardial infarction-related events. Improved procedural technique with BVS (more aggressive plaque modification before BVS implantation, routine high-pressure non-compliant balloon post-dilatation to ensure adequate scaffold expansion, and more frequent use of intravascular imaging to optimise lesion coverage and scaffold dimensions) might further reduce thrombosis rates. Nonetheless, neither cardiac nor all-cause mortality were increased with BVS, and all measures of clinical effectiveness at 1-year were similar with BVS and CoCr-EES, which was indicative of the similar in-segment luminal dimensions achieved.[33] Combined with the overall similar rates of the patient-oriented composite endpoint and device-oriented composite endpoint, these findings support the safety and effectiveness of BVS use at 1 year for treatment of patients with stable coronary artery disease and stabilised acute coronary syndromes.

Several limitations of this meta-analysis should be mentioned. We excluded two small randomised trials (TROFI II and EVERBIO II, with reported follow-up data in 189 and 158 patients, respectively) from the primary meta-analysis because both had follow-up duration shorter than 1 year, and the TROFI II trial restricted enrolment to patients with ST-elevation myocardial infarction.[12,13] However, in a sensitivity analysis, the main study-level treatment-related effects were not changed substantially by the inclusion of these two studies. Second, although this is the largest study so far of BVS versus metallic drug-eluting stents, even the present analysis of 3389 patients (or 3736 patients if we include those from TROFI II and EVERBIO II) does not have sufficient power to detect very small differences in low frequency events, such as device thrombosis and mortality. In this regard, insights into the precision of the present study can be gained by examining the 95% CIs around the point estimates of the treatment effects. Third, the subgroup analysis is inherently underpowered, and interaction testing was not adjusted for multiple comparisons. Consequently, all subgroup findings should be regarded as hypothesis-generating, although several borderline significant interactions were observed which deserve further study. Fourth, since the completion of these studies, the importance of optimum technique for BVS implantation has become more widely appreciated, with a premium placed on aggressive lesion preparation, optimum device sizing, and routine post-dilatation to achieve maximal scaffold expansion. Further research is needed to ascertain the extent to which these measures improve peri-procedural and 1-year outcomes of BVS. Additionally, the slightly greater use of prasugrel and ticagrelor with BVS compared with CoCr-EES might have reduced scaffold thrombosis rates. Fifth, all the trials included in the present study excluded very high-risk patients and those with complex lesions, such as chronic total occlusions, very long lesions, bifurcations with large side branches, and ST-elevation myocardial infarction (except for TROFI II). Dedicated studies are needed to establish the performance of BVS in these scenarios. Sixth, the present study results apply strictly to the first-generation BVS, and not to other polymeric or metal-based bioresorbable scaffolds. A second-generation BVS with thinner struts and improved expansion characteristics is under development, and might improve outcomes compared with the device studied in this report. Finally, the ultimate benefit–risk assessment of BVS as compared with metallic drug-eluting stents awaits the 5-year results from ongoing large-scale trials, especially the ABSORB IV trial.

In conclusion, in the present meta-analysis of randomised trials of the Absorb BVS versus Xience CoCr-EES, BVS resulted in non-significantly different overall rates of composite patient-oriented and device-oriented adverse events at 1-year follow-up.

Contributors

GWS designed the study, interpreted the data and drafted the report. ZZ (Abbott Vascular) did the statistical analyses. All authors provided critical interpretation of the data and the draft report for revision. GWS controlled the decision to submit for publication and accepts responsibility for the integrity of the study. All authors have approved the final version and agree with its content and conclusions.

Declaration of interests

GWS has served as a consultant to Osprey, Reva, Boston Scientific, AstraZeneca, Eli Lilly–Daiichi Sankyo partnership, InspireMD, TherOx, Atrium, Volcano, InfraReDx, Miracor, Velomedix, CSI, and Matrizyme, and has stock or stock options with Biostar family of funds, MedFocus family of funds, Caliber, Guided Delivery Systems, Micardia, VNT, Cagent, and Qool Therapeutics. RG has a research grant from Abbott Vascular. DJK has served as a consultant to Harvard Clinical Research Institute, Sanofi-Aventis, Boston Scientific, Abbott Vascular, and Ablative Solutions Inc. SGE has served as a consultant to Abbott Vascular. TK is an advisory board member for Abbott Vascular. W-FC, JJ-M, XS, and ZZ are full-time employees of Abbott Vascular; YO and PWS declare no competing interests.

References

1 Windecker S, Stortecky S, Stefanini GG, et al. Revascularisation versus medical treatment in patients with stable coronary artery disease: network meta-analysis. *BMJ* 2014; **348:** g3859.

2 Bangalore S, Kumar S, Fusaro M, et al. Short-and long-term outcomes with drug-eluting and bare-metal coronary stents: a mixed-treatment comparison analysis of 117 762 patient-years of follow-up from randomized trials. *Circulation* 2012; **125:** 2873–91.

3 Palmerini T, Benedetto U, Biondi-Zoccai G, et al. Long-term safety of drug-eluting and bare-metal stents: evidence from a comprehensive network meta-analysis. *J Am Coll Cardiol* 2015; **65:** 2496–507.

4 Gada H, Kirtane AJ, Newman W, et al. Five-year results of a randomized comparison of XIENCE V everolimus-eluting and TAXUS paclitaxel-eluting stents: final results from the SPIRIT III trial. *JACC Cardiovasc Interv* 2013; **6:** 1263–66.

5 Smits PC, Vlachojannis GJ, McFadden EP, et al. Final 5-year follow-up of a randomized controlled trial of everolimus- and paclitaxel-eluting stents for coronary revascularization in daily practice: the COMPARE trial (a trial of everolimus-eluting stents and paclitaxel stents for coronary revascularization in daily practice). *JACC Cardiovasc Interv* 2015; **8:** 1157–65.

6 Taniwaki M, Stefanini GG, Silber S, et al. 4-year clinical outcomes and predictors of repeat revascularization in patients treated with new-generation drug-eluting stents: a report from the RESOLUTE All-Comers trial (a randomized comparison of a zotarolimus-eluting stent with an everolimus-eluting stent for percutaneous coronary intervention). *J Am Coll Cardiol* 2014; **63:** 1617–25.

7 Mauri L, Kereiakes DJ, Yeh RW, et al. Twelve or 30 months of dual antiplatelet therapy after drug-eluting stents. *N Engl J Med* 2014; **371:** 2155–66.

8 Serruys PW, Chevalier B, Dudek D, et al. A bioresorbable everolimus-eluting scaffold versus a metallic everolimus-eluting stent for ischaemic heart disease caused by de-novo native coronary artery lesions (ABSORB II): an interim 1-year analysis of clinical and procedural secondary outcomes from a randomised controlled trial. *Lancet* 2015; **385:** 43–54.

9 Kimura T, Kozuma K, Tanabe K, et al. A randomized trial evaluating everolimus-eluting Absorb bioresorbable scaffolds vs. everolimus-eluting metallic stents in patients with coronary artery disease: ABSORB Japan. *Eur Heart J* 2015; published online Sept 1. http://dx.doi.org/10.1093/eurheartj/ehv435.

10 Gao R, Yang Y, Han Y, et al. Randomized comparison of everolimus-eluting absorb bioresorbable vascular scaffolds vs. everolimus-eluting metallic stents in patients with coronary artery disease: the ABSORB China trial. *J Am Coll Cardiol* 2015; **66:** 2298–309.

11 Ellis SG, Kereiakes DJ, Metzger C, et al. Everolimus-eluting bioresorbable vascular scaffolds in patients with coronary artery disease: the ABSORB III trial. *N Engl J Med* 2015; **373:** 1905–15.

12 Puricel S, Arroyo D, Corpataux N, et al. Comparison of everolimus- and biolimus-eluting coronary stents with everolimus-eluting bioresorbable vascular scaffolds. *J Am Coll Cardiol* 2015; **65:** 791–801.

13 Sabaté M, Windecker S, Iñiguez A, et al. Everolimus-eluting bioresorbable stent vs. durable polymer everolimus-eluting metallic stent in patients with ST-segment elevation myocardial infarction: results of the randomized ABSORB ST-segment elevation myocardial infarction-TROFI II trial. *Eur Heart J* 2015; published online Sept 23. http://dx.doi.org/10.1093/eurheartj/ehv500.

14 Moussa ID, Klein LW, Shah B, et al. Consideration of a new definition of clinically relevant myocardial infarction after coronary revascularization: an expert consensus document from the Society for Cardiovascular Angiography and Interventions (SCAI). *J Am Coll Cardiol* 2013; **62:** 1563–70.

15 Kereiakes DJ, Ellis SG, Popma JJ, et al. Evaluation of a fully bioresorbable vascular scaffold in patients with coronary artery disease: design of and rationale for the ABSORB III randomized trial. *Am Heart J* 2015; **170:** 641–51.

16 Cutlip DE, Windecker S, Mehran R, et al. Academic Research Consortium. Clinical end points in coronary stent trials: a case for standardized definitions. *Circulation* 2007; **115:** 2344–51.

17 Lansky AJ, Dangas G, Mehran R, et al. Quantitative angiographic methods for appropriate endpoint analysis, edge-effect evaluation, and prediction of recurrent restenosis after coronary brachytherapy with gamma irradiation. *J Am Coll Cardiol* 2002; **39:** 274–80.

18 Sweeting MJ, Sutton AJ, Lambert PC. What to add to nothing? Use and avoidance of continuity corrections in meta-analysis of sparse data. *Stat Med* 2004; **23:** 1351–75.

19 Peduzzi P, Concato J, Kemper E, et al. A simulation study of the number of events per variable in logistic regression analysis. *J Clin Epidemiol* 1996; **49:** 1373–79.

20 Viechtbauer W. Conducting meta-analyses in R with the metafor package. *J Stat Softw* 2010; **36:** 1–48. http://www.jstatsoft.org/v36/i03/ (accessed Sept 13, 2015).

21 R Core Team. R: a language and environment for statistical computing. 2015. http://www.R-project.org/ (accessed Sept 13, 2015).

22 Joner M, Finn AV, Farb A, et al. Pathology of drug-eluting stents in humans: delayed healing and late thrombotic risk. *J Am Coll Cardiol* 2006; **48:** 193–202.

23 Otsuka F, Vorpahl M, Nakano M, et al. Pathology of second-generation everolimus-eluting stents versus first-generation sirolimus- and paclitaxel-eluting stents in humans. *Circulation* 2014; **129:** 211–23.

24 Ong P, Athanasiadis A, Perne A, et al. Coronary vasomotor abnormalities in patient with stable angina after successful stent implantation but without in-stent restenosis. *Clin Res Cardiol* 2014; **103:** 11–19.

25 Serruys PW, Garcia-Garcia HM, Onuma Y. From metallic cages to transient bioresorbable scaffolds; change in paradigm of coronary revascularization in the upcoming decade? *Eur Heart J* 2012; **33:** 16–25.

26 Lane JP, Perkins LE, Sheehy AJ, et al. Lumen gain and restoration of pulsatility after implantation of a bioresorbable vascular scaffold in porcine coronary arteries. *JACC Cardiovasc Interv* 2014; **7:** 688–95.

27 Serruys PW, Ormiston JA, Onuma Y, et al. A bioabsorbable everolimus-eluting coronary stent system (ABSORB): 2-year outcomes and results from multiple imaging methods. *Lancet* 2009; **373:** 897–910.

28 Serruys PW, Onuma Y, Garcia-Garcia HM, et al. Dynamics of vessel wall changes following the implantation of the absorb everolimus-eluting bioresorbable vascular scaffold: a multi-imaging modality study at 6, 12, 24 and 36 months. *EuroIntervention* 2014; **9:** 1271–84.

29 Simsek C, Karanasos A, Magro M, et al. Long-term invasive follow-up of the everolimus-eluting bioresorbable vascular scaffold: five-year results of multiple invasive imaging modalities. *EuroIntervention* 2014; published online Oct 28. DOI:10.4244/EIJY14M10_12.

30 Brugaletta S, Radu MD, Garcia-Garcia HM, et al. Circumferential evaluation of the neointima by optical coherence tomography after ABSORB bioresorbable vascular scaffold implantation: can the scaffold cap the plaque? *Atherosclerosis* 2012; **221:** 106–12.

31 Bourantas CV, Garcia-Garcia HM, Diletti R, Muramatsu T, Serruys PW. Early detection and invasive passivation of future culprit lesions: a future potential or an unrealistic pursuit of chimeras? *Am Heart J* 2013; **165:** 869–881.

32 Nakazawa G, Finn AV, Joner M, et al. Delayed arterial healing and increased late stent thrombosis at culprit sites after drug-eluting stent placement for acute myocardial infarction patients: an autopsy study. *Circulation* 2008; **118:** 1138–45.

33 Pocock SJ, Lansky AJ, Mehran R, et al. Angiographic surrogate end point in drug-eluting stent trials: a systemic evaluation based on individual patient data from 11 randomized, controlled trials. *J Am Coll Cardiol* 2008; **51:** 23–32.